

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
21 August 2003 (21.08.2003)

PCT

(10) International Publication Number  
**WO 2003/068732 A3**

(51) International Patent Classification<sup>7</sup>: **C07D 223/16**,  
A61K 31/395, A61P 25/18, C07D 217/02, 209/44, 409/12,  
405/12

[GB/GB]; GlaxoSmithKline, New Frontiers Science Park  
South, Third Avenue, Harlow, Essex CM19 5AW (GB).

(21) International Application Number:  
PCT/EP2003/001544

(74) Agent: **MCKINNEL, Denise**; GlaxoSmithKline,  
CN925.1, 980 Great West Road, Brentford, Middlesex  
TW8 9GS (GB).

(22) International Filing Date: 13 February 2003 (13.02.2003)

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,  
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,  
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,  
MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE,  
SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,  
VC, VN, YU, ZA, ZM, ZW.

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
0203435.3 13 February 2002 (13.02.2002) GB  
0204721.5 28 February 2002 (28.02.2002) GB

(84) Designated States (*regional*): ARIPO patent (GH, GM,  
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),  
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,  
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI,  
SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN,  
GQ, GW, ML, MR, NE, SN, TD, TG).

(71) Applicant (*for all designated States except US*): **GLAXO  
GROUP LIMITED** [GB/GB]; Glaxo Wellcome House,  
Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **COOPER, David**,  
Gwyn [GB/GB]; GlaxoSmithKline, New Frontiers Sci-  
ence Park South, Third Avenue, Harlow, Essex CM19  
5AW (GB). **FORBES, Ian, Thomson** [GB/GB]; Glaxo-  
SmithKline, New Frontiers Science Park South, Third  
Avenue, Harlow, Essex CM19 5AW (GB). **GRIBBLE**,  
**Andrew, Derrick** [GB/GB]; GlaxoSmithKline, New  
Frontiers Science Park South, Third Avenue, Harlow,  
Essex CM19 5AW (GB). **LIGHTFOOT, Andrew, P**

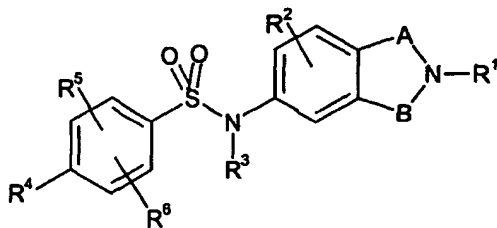
Published:

— with international search report

(88) Date of publication of the international search report:  
8 April 2004

*For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.*

(54) Title: BENZENESULFONAMIDE DERIVATIVES AND THEIR USE AS DOPAMINE D3 AND D2 RECEPTOR LIGANDS



(I)

(57) Abstract: The invention provides compounds of formula (I) wherein A and B represent the groups  $-(CH_2)_m-$  and  $-(CH_2)_n-$  respectively;  $R^1$  represents hydrogen or  $C_{1-6}$ alkyl;  $R^2$  represents hydrogen, halogen, hydroxy, cyano, nitro, hydroxy $C_{1-6}$ alkyl, trifluoromethyl, trifluoromethoxy,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $-(CH_2)_pC_{3-6}$ cycloalkyl,  $-(CH_2)_pC_{3-6}$ cycloalkyloxy,  $-COC_{1-6}$ alkyl,  $-SOC_{1-6}$ alkyl,  $-SOC_{1-6}$ alkyl,  $-S-C_{1-6}$ alkyl,  $-COC_{1-6}$ alkyl,  $-CO_2NR^7R^8$ ,  $-SO_2NR^7R^8$ ,

$-(CH_2)_pNR^7R^8$ ,  $-(CH_2)_pNR^7COR^8$ , optionally substituted aryl, optionally substituted heteroaryl or a fused bicyclic heterocyclic ring system;  $R^3$  represents hydrogen or  $C_{1-6}$ alkyl;  $R^4$  represents halogen, trifluoromethyl, trifluoromethoxy,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $-(CH_2)_pC_{3-6}$ cycloalkyl or  $-(CH_2)_pC_{3-6}$ cycloalkyloxy;  $R^5$  and  $R^6$  each independently represent hydrogen, halogen, hydroxy, cyano, nitro, hydroxy $C_{1-6}$ alkyl, trifluoromethyl, trifluoromethoxy,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy,  $-(CH_2)_pC_{3-6}$ cycloalkyl,  $-(CH_2)_pC_{3-6}$ cycloalkyloxy,  $-COC_{1-6}$ alkyl,  $-SO_2C_{1-6}$ alkyl,  $-SOC_{1-6}$ alkyl,  $-S-C_{1-6}$ alkyl,  $-CO_2C_{1-6}$ alkyl,  $-CO_2NR^7R^8$ ,  $-SO_2NR^7R^8$ ,  $-(CH_2)_pNR^7R^8$ ,  $-(CH_2)_pNR^7COR^8$ , optionally substituted aryl, optionally substituted heteroaryl or a fused bicyclic heterocyclic ring system;  $R^7$  and  $R^8$  each independently represent hydrogen or  $C_{1-6}$ alkyl; m and n independently represent an integer selected from 1 and 2; p independently represents an integer selected from 0, 1, 2 and 3; or a pharmaceutically acceptable salt or solvate thereof, with the proviso that the compounds 4-methyl-N-(1,2,3,4-tetrahydroisoquinolin-6-yl)-benzenesulfonamide, 7-(4-chlorophenyl)sulfonamido-1,2,3,4-tetrahydroisoquinoline hydrochloride and N-(2-ethyl-5-isoindolyl)-p-toluenesulfonamide are excluded. The compounds are useful in therapy, in particular as antipsychotic agents.

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/01544

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D223/16 A61K31/395 A61P25/18 C07D217/02 C07D209/44  
C07D409/12 C07D405/12

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97 45403 A (PHARMACIA & UPJOHN COMPANY) 4 December 1997 (1997-12-04) claims 1,31	1,3,7
A	WO 00 21951 A (SMITHKLINE BEECHAM PLC) 20 April 2000 (2000-04-20) claims 1,7,8	1,3,7
A	WO 98 50364 A (SMITHKLINE BEECHAM PLC) 12 November 1998 (1998-11-12) claims 1,11,12	1,3,7
A	US 5 939 451 A (MICHAEL BÖS ET AL.) 17 August 1999 (1999-08-17) column 1	1,3
	--- -/-	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"Z" document member of the same patent family

Date of the actual completion of the international search

10 November 2003

Date of mailing of the international search report

04/12/2003

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Van Bijlen, H

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/01544

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 03 068751 A (GLAXO GROUP LTD.) 21 August 2003 (2003-08-21) claims; examples 5,6,10-12,16 -----	1,3,7

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP 03/01544

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  

Although claims 9-10 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/01544

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9745403	A	04-12-1997	AT 247639 T	15-09-2003
			AU 720414 B2	01-06-2000
			AU 3060197 A	05-01-1998
			CN 1217711 A	26-05-1999
			CZ 9803701 A3	12-05-1999
			DE 69724259 D1	25-09-2003
			EP 0923542 A1	23-06-1999
			FI 982572 A	27-11-1998
			JP 2000511529 T	05-09-2000
			KR 2000016147 A	25-03-2000
			NO 985599 A	30-11-1998
			NZ 332538 A	23-02-2001
			PL 330207 A1	26-04-1999
			RU 2185372 C2	20-07-2002
			SK 148898 A3	13-03-2000
			WO 9745403 A1	04-12-1997
			US 6084130 A	04-07-2000
WO 0021951	A	20-04-2000	AU 761018 B2	29-05-2003
			AU 1038100 A	01-05-2000
			BG 105467 A	30-11-2001
			BR 9914370 A	27-11-2001
			CA 2346689 A1	20-04-2000
			CN 1329609 T	02-01-2002
			CZ 20011270 A3	12-09-2001
			WO 0021951 A1	20-04-2000
			EP 1119563 A1	01-08-2001
			HU 0104280 A2	28-03-2002
			JP 2002527433 T	27-08-2002
			NO 20011745 A	06-06-2001
			NZ 511018 A	26-09-2003
			PL 347237 A1	25-03-2002
			SK 4782001 A3	06-11-2001
			TR 200101025 T2	21-09-2001
			US 6605607 B1	12-08-2003
			ZA 200102758 A	04-06-2002
WO 9850364	A	12-11-1998	AU 725491 B2	12-10-2000
			AU 7651898 A	27-11-1998
			BR 9809591 A	11-09-2001
			CN 1261350 T	26-07-2000
			WO 9850364 A1	12-11-1998
			EP 0983244 A1	08-03-2000
			HU 0003608 A2	28-03-2001
			JP 2002501506 T	15-01-2002
			NO 995338 A	02-11-1999
			PL 336628 A1	03-07-2000
			TR 9902724 T2	21-04-2000
			US 6465485 B1	15-10-2002
			ZA 9803659 A	01-11-1999
US 5939451	A	17-08-1999	AT 205714 T	15-10-2001
			AU 694696 B2	23-07-1998
			AU 2841697 A	22-01-1998
			BR 9703788 A	17-11-1998
			CA 2209018 A1	28-12-1997
			CN 1170574 A ,B	21-01-1998
			CZ 9702002 A3	14-01-1998

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/01544

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5939451	A	DE 59704640 D1	25-10-2001
		DK 815861 T3	21-01-2002
		EP 0815861 A1	07-01-1998
		ES 2163071 T3	16-01-2002
		HK 1007865 A3	30-04-1999
		HK 1007865 A1	03-05-2002
		HR 970349 A1	30-04-1998
		HU 9701096 A2	01-02-1999
		IL 121141 A	23-12-2001
		JP 3032176 B2	10-04-2000
		JP 10067734 A	10-03-1998
		KR 260480 B1	01-07-2000
		NO 972983 A	29-12-1997
		NZ 328146 A	28-10-1999
		PL 320822 A1	05-01-1998
		PT 815861 T	28-02-2002
		RU 2192257 C2	10-11-2002
		SG 77139 A1	19-12-2000
WO 03068751	A	21-08-2003	
		WO 03068751 A1	21-08-2003
		WO 03068752 A1	21-08-2003